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UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: **Letts et al.**

Application No: **10/718,060**

Group Art Unit: **1626**

Filed: **June 10, 2003**

Examiner: **Rebecca L. Anderson**

For: **Nitrosated and/or Nitrosylated Cyclooxygenase-2 Inhibitors, Compositions and Methods of Uses**

Attorney Docket No: **102258.157 US1**

Commissioner of Patents
PO Box 1450
Alexandria, VA 22313-1450

Supplemental Response to Restriction Requirement

I. Introductory Comments

This response is submitted in reply to the Office Communication dated September 19, 2005 for which a response is due on or before October 19, 2005.

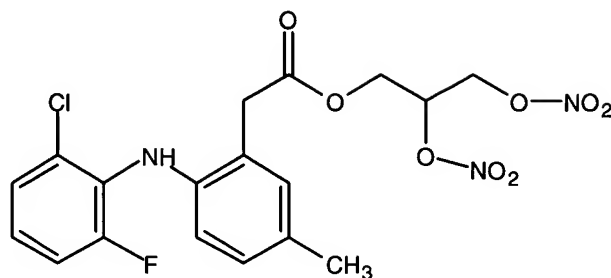
No fee is believed to be due; however, the Commissioner is authorized to charge any necessary fees or credit any overpayments to Deposit Account No. 08-0219 to maintain the pendency of the present application.

II. Election of Species

The Examiner asserts that Applicant's election of the compound of Formula (V) is improper as it is specifically excluded in the proviso on page 20 of the specification.

Applicants respectfully disagree and respectfully submit that the species elected by Applicant, the nitrosated cyclooxygenase inhibitor compound of Formula (V), 2,3-bis(nitroxy)propyl 2(2-((2-chloro-6-fluorophenyl)amino)5-methylphenyl)acetate, is not encompassed by the proviso in the specification.

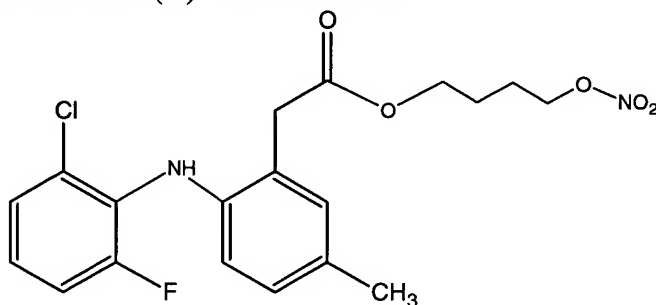
The compound of Formula (V) has the structure:



(V)

The proviso in the specification excludes nitrooxy lower alkyl esters, such as 4-(nitrooxy)butyl {2-[(2-chloro-6-fluorophenyl)amino]-5-methylphenyl} acetate of Formula (A), as disclosed in WO 99/11605.

The compound of Formula (A) has the structure:



(A)

Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 executed by David S. Garvey, Ph.D. (hereafter the “Garvey Declaration”). The Garvey Declaration supports and provides evidence that one of skill in the art would appreciate that the compound elected by Applicants is a substituted nitrooxy lower alkyl ester that is **not** encompassed by the proviso in the specification. In particular, the Garvey Declaration at paragraph no. 7 states:

“It is my opinion that in the present application by excluding nitrooxy lower alkyl esters, Applicants **did not** exclude nitrooxy lower alkyl ester compounds that contain more than one nitrooxy group, such as, for example, bis(nitrooxy) lower alkyl ester compounds, and the like, or other poly(nitrooxy) lower alkyl ester compounds such as, for example lower alkyl ester compounds that contain more than one nitrooxy group, and the like.”

It is Dr. Garvey's opinion that the definition of a lower alkyl group in the specification of WO 99/11605 does not contemplate a substituted lower alkyl group. (See Garvey Declaration at paragraph 8.)

Additionally, Applicants respectfully submit that one skilled in the art would appreciate that a nitrooxy lower alkyl ester compound is a mono(nitroxy) compound that contains only one nitrooxy group and does not encompass a bis(nitroxy) alkyl ester compound that contains two nitrooxy groups or other poly(nitrooxy) alkyl ester compounds that contain more than one nitrooxy group. (See Garvey Declaration at paragraph 9).

Furthermore, one skilled in the art would appreciate that a compound that contains only one nitrooxy group has different biological properties as a compound that contains two nitrooxy groups. For example, the Garvey Declaration presents recent studies by Young et al, *Biochemical Pharmacology* 70: 1343-1351 (2005), that showed that a bis(nitroxy) alkyl ester of naproxen, produces more absolute NO_x, mainly as a nitrite, than a nitrooxy alkyl ester of naproxen containing only one nitrooxy group, that produces NO_x mainly as a nitrate. See Garvey Declaration at paragraph no. 10.

The Garvey Declaration at paragraph 15 states:

“the data from Young et al shows that a nitrooxy alkyl ester compound i.e. a compound containing only one nitrooxy group, has different biological properties than a bis(nitroxy) alkyl ester compound i.e. a compound containing two nitrooxy groups”.

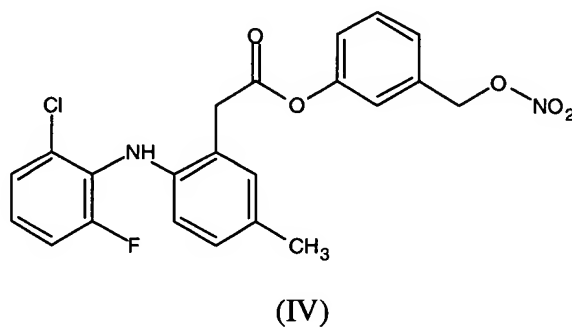
It is Dr. Garvey's opinion that based on the teachings in WO 99/11605 and in Young et al, one skilled in the art would conclude that the compound of Formula (V) of the present application is **not** encompassed by the nitrooxy lower alkyl esters, such as, for example, the 4-(nitrooxy)butyl {2-[(2-chloro-6-fluorophenyl)amino]-5-methylphenyl}acetate of Formula (A) disclosed in WO 99/11605.

In view of the above, Applicants respectfully submit that the species elected by the Applicant in the response submitted on July 8, 2005, is proper and respectfully request the objection be withdrawn.

III. Additional Election of Species

In order to further prosecution, Applicants elect the nitrosated cyclooxygenase inhibitor compound of Formula (IV), 3-((nitroso)methylphenyl) 2(2-((2-chloro-6- fluorophenyl) amino)5-methylphenyl)acetate, with traverse.

This compound has the structure:



The compound is disclosed in the specification at page 22, lines 9-14.

IV. Conclusion

Applicants respectfully request that the objection in the Office Communication be withdrawn and the Examiner examines the compound of Formula (V) as the elected species.

An early and favorable consideration and allowance of the pending claims is respectfully requested.

Respectfully submitted,

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Date: October 19, 2005
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